IN THE U.S. PATENT AND TRADEMARK OFFICE

U.S. Appl. No.:	10/563,094	Confirmation No.:	8178
Title:	ANTIBODIES TO THE FUEL OXYGENATE MTBE AND USE THEREOF IN IMMUNOASSAYS		
Inventor(s):	Selwayan Saini, et al.		
Filed:	June 19, 2006		
Art Unit:	1641		
Examiner:	Haq, Shafiqul		
Docket No.:	P08828US00/BAS		
Customer No.:	000881		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF DAVID C. CULLEN, PH.D.
PURSUANT TO 37 C.F.R. §1.132

Sir:

I, David C. Cullen, declare and state as follows:

1. I am currently a Professor of Bioanalytical Technology at Cranfield University, Cranfield, MK43 0AL, United Kingdom.

2. My formal training is in biochemistry. I have a B.Sc. Honours degree in biochemistry from the University of East Anglia (England) and a Ph.D. from the University of Cambridge (England), where I also carried out post-doctoral studies. I moved to Cranfield University in 1994 initially as a lecturer in biophysics and biosensors. The production of small-molecule protein conjugates using spacer

molecules is an important part of my current work that involves the development of antibodies to small-molecules and which would be indicative of life on Mars. This work forms part of a large international project to develop an antibody-based instrument to go on a European Space Agency rover mission (ExoMars) to Mars to search for evidence of life.

3) I am familiar with the above-referenced application, which is directed toward methods of generating antibodies for assaying a fuel oxygenate in which the antibodies are produced by conjugating a carrier protein to a hapten via a spacer and a group that is capable of binding to the carrier protein. My understanding is that in conjunction with this application, the Examiner has made the assertion that the terms "spacer" and "group capable of bind to a carrier protein" are unclear and that it is not apparent what compounds or structures may be encompassed by those terms. For reasons as stated below, such is not the case.

4) To the contrary, procedures for attaching small molecules to proteins so that antibodies can be produced have been very well known for many years. It is common for there to be a moiety termed a "spacer" interposed between the small molecule and the protein. This commonly improves the ability of the conjugate to elicit production of antibodies that are specific to the small molecule (often called the hapten when described in context of antibody production). The nature of the spacer generally has some effect on this ability. However, it is an entirely routine matter,

well within the capacity of scientists in the field, to produce conjugates containing a range of spacers and screen them for suitability.

5) Indeed, a book entitled "Bioconjugate Techniques" was published by Elsevier in 1996 (ISBN: 978-0-12-342335-1) and is a compilation of known techniques for producing "bioconjugates" including hapten-protein conjugates. A true and correct copy of relevant portions of that book are attached hereto as Exhibits A-C, and include: a copy of the inside front cover of the book which gives bibliographical information (Exhibit A); a copy of Chapter 9 of the book, entitled "Preparation of hapten-carrier immunogen conjugates" (Exhibit B); and a copy of Chapter 5 of the book, entitled "Heterobifunctional cross-linkers" (Exhibit C).

6) Chapter 9 is specifically about the preparation of hapten-carrier immunogen conjugates and shows that this was a common procedure by 1996. The use of proteins as carriers is discussed on pages 421-427. Further, there are also many references to the use of spacers, e.g. page 441, lines 4 and 6, and page 443, 2 lines from foot of main text. Chapter 9 also includes an extensive discussion of suitable groups capable of binding to the carrier protein, particularly in Section 6 beginning on page 446, Section 7 beginning on page 453 and Section 8 beginning on page 454.

7) Chapter 5 of the book contains an extensive discussion of the choice of a "cross-bridge or spacer", e.g. on page 229, lines 10-15.

8) Accordingly, to the extent that the Examiner has asserted that the terms "spacer" and "group capable of binding to a carrier protein" would be unclear or that it would not be apparent what compounds or structures may be encompassed by those terms, such assertions are simply not true. To the contrary, as shown in excerpts from the "Bioconjugate Techniques" book attached hereto as Exhibits A-C and referred to above, scientists in the field are very familiar with procedures for attaching molecules to proteins, and it is an entirely routine matter to select a suitable "spacer" or "group capable of binding to a protein", with due regard to the particular protein being used, and the nature of the molecule to be attached to it.

9) I hereby declare that all the statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

30th September 2009

Date

David C. Cullen